

### REMARKS

Of Claims 1-11, which are in the application, Claims 10 and 11 have been withdrawn from the application pursuant to a restriction requirement and Claims 1-9 have been rejected. Applicants address hereunder the restriction and rejection.

#### Restriction of the Claims

The Examiner requests the restriction requirement under 35 USC 121 to one of the following inventions, as follows:

- I. Claims 1-9 in part when the end product is a 2-alkyl-aryloxaziridine where X is a C<sub>6</sub>-C<sub>12</sub> aryl, drawn to methods of making, classified in class 548, various subclasses.
- II. Claims 1-9 in part when the end product is a heteroaryloxaziridine where X is a heterocycle, drawn to methods of making, classified in class 548, various subclasses.
- III. Claims 10 and 11, drawn to compounds, classified in class 548, subclass 959.

While confirming their provisional election of the claims of Group 1, Applicants submit that it would be more expedient to search and examine all the claims, which are in the same class. For the search relating to claims of one group would constitute a search relating to the other claims. Therefore, Applicants urge a search and examination of all the claims at the same time.

#### Rejection of the Claims

Claims 1-9 stand rejected under 35 USC 103(a) as being unpatentable over Krimm et al (US 2,784,182) in view of Schirmann et al (US 3,819,653). Claims 1-7 stand rejected under 35 USC 103(a) as being unpatentable over Bulachkova et al (abstract only of Russian paper) in view of Schirmann et al. Applicants traverse the rejection for failure to make a prima facie obviousness in that the references do not provide a basis for the proposed modification of adding water to water-immiscible solvents.

### Statement of the Basis of the Rejection

The claims stand rejected over the primary references, Krimm and Bulachkova, based on the Examiner's contention that:

"Krimm, et al. disclose the oxidation of aldimines (or Schiff's bases) by aromatic percarboxylic acids in the presence of water-miscible base (potassium carbonate, for example; see column 8, line 30 in Example 15) at a temperature of from 0°C – 100°C."

"Bulachkova, et al. disclose the preparation of substituted alkyl-aryl-oxaziridines from oxidation of aldimines (Schiff bases) via an aromatic peracid at a temperature < 30°C (see abstract provided.)"

Acknowledging that the claims differ from the primary references, the Examiner cites the secondary reference, Schirmann et al for the proposition that:

"Schirmann, et al. disclose a method for preparing substituted oxaziridines by oxidation of N-alkyl-arylaldimines with peracids, in the presence of water-soluble solvents and at a temperature < 30°C in an aqueous environment (column 2, lines 54-58)".

The Examiner contends that:

"One of ordinary skill in the art would have been motivated to conduct the instantly claimed process in an aqueous environment in view of the Schirmann reference when said reference specifically points out that an aqueous environment is advantageous in the reaction (column 2, lines 54-58)".

"Furthermore, optimization of reaction conditions such as temperature or concentration or other process conditions of a known process or routine experimentation common in the art does not impart patentability unless the recited ranges are critical, i.e., they produce a new and unexpected result. *In re Aller, et al.*, (CCPA 1955) 220 F2nd 454, 105 USPQ 233."

In essence the rejection is based on the grounds that the difference between the claims and the prior art resides in the failure of the primary reference to teach the claim-element of adding water to water-miscible solvents, and that this addition is suggested by the secondary reference. Applicants traverse the rejection for failure to establish a prima facie case in that the proposed combination of references would not have led to the claimed process with a reasonable expectation of success. More specifically, the Examiner has not advanced evidence or practical reason of record, which would have led the skilled artisan to the proposed combination of water with a water-immiscible solvent. For the claimed process, such a combination would be unsatisfactory.

Hence, there is presented an issue of:

- (1) whether there is a basis of record which would have led the skilled artisan with a reasonable expectation of success to modify Krimm's process which involved the use of water-immiscible solvents by adding water, where the pertinent art teaches that the presence of water is fraught with problems.
- (2) whether the modification would have led to the claims.

To establish prima facie obviousness, there must be a basis in the art for modifying the claims with a reasonable expectation of success, In re Fine 5 USPQ2d 1956 (Fed Cir. 1988). The record is devoid of evidence or practical reason of record, which would have led the skilled artisan to modify the references with a reasonable expectation of success.

Applicants traverse the rejection because the desirability of conducting reactions in an aqueous medium does not suffice as a basis for modifying the primary references to this invention. To suffice as a basis for making the proposed modification, it is necessary to ascertain whether the teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination or other modifications, In re Lintner 173 USPQ 560 (CCPA 1972). In this case, the record does not point to how the skilled artisan having the references before him would have modified the prior art to the claims.

The mere fact that the references can be combined or modified does not render the proposed combination obvious unless the prior art suggests the desirability of making the combination as discussed above.

At any rate, the proposed combination of references does not lead to the claims encompassing a mixture of water and a water-miscible solvent. Adding more water to the process of Krimm would have led to an unsatisfactory combination of water and water-immiscible organic solvent. Where the proposed modification would be unsatisfactory, it cannot be said to render the claims obvious, In re Gordon 221 USPQ 1125 (Fed Cir. 1984). Differently put, a person skilled in the art would not have been motivated to add more water in process of Krimm, as it is well known that the presence of water is detrimental for the reaction of imines with per-compounds. In the presence of acids and water, the imines used as starting materials tend to hydrolyze, thereby lowering the yield achieved. Additionally, the presence of water and acid results in a hydrolytic cleavage of the oxaziridines formed into corresponding aldehyde and the corresponding NO-substituted hydroxylamine. The latter is easily oxidized to give an undesired nitroso-compound as by-product. These side-reactions additionally lower the yield (see the captioned application, at page 2, lines 12-15 and lines 17-23). These undesired consequences relating to the presence of water are reflected by the poor yields achieved in the Krimm process.

Applicants further traverse the rejection based on the assertion that the addition of water constitutes optimization. It is well established that a particular parameter must first be recognized as a result-effective, i.e., a variable which achieves a recognized result before the determination of the optimum or workable range of said variable, In re Antonie 195 USPQ 6 (CCPA 1997). In this case, the record does not show that the addition of water was recognized as a result-effective variable. Therefore, a basis for arguing optimization has not been established. In view of the foregoing, Applicants submit that Krimm in view of Schirmann does not support a case of prima facie obviousness.

Bulachkova discloses the preparation of oxaziridines by reacting imines with perbenzoic acid. This reaction is carried out as a phase transfer epoxidization. This means that the reaction system comprises water and a non-water miscible organic solvent, as well as a phase-transfer catalyst. Such two-phase systems without a phase transfer-catalyst are known in the preparation of oxaziridines, as acknowledged by the citation of WO-A-00/02848 at page 2, line 25ff of the captioned application. This process is disadvantaged if up-scaling of the reaction is intended.

There is no basis in Schirmann for modifying the two-phase system of Bulachkova in order to overcome its disadvantages such those associated with scaling up the reaction. Therefore Bulachkova in view of Schirmann fails to support a case for prima facie obviousness.


At any rate, a presumption of obviousness is rebutted by the marked improvements that attend the process. The combination of water with water-miscible solvent results in the observed high yields of the desired oxaziridines. Additionally the addition of a base during the reaction – and not afterwards - results in further improvement of the yield, by reducing the acidic side reactions described above. Also, the presence of water according to the present invention makes the handling of the percarboxylic acid safer.

In view of the foregoing, Applicants submit that the Examiner is justified in allowing the claims remaining in the application.

Respectfully submitted,

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